

Impact of Socioeconomic Deprivation on Mortality in People with Haemorrhagic Stroke: *a population-based cohort study*

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ABSTRACT

Purpose: Socioeconomic deprivation (SED) has an effect on many health outcomes, including ischaemic stroke, however its impact on mortality after haemorrhagic stroke remains unclear, particularly in the long run. We examined this association in a multi-ethnic population in the UK.

Design: We examined data from 782 patients with first-ever haemorrhagic stroke, collected by the South London Stroke Register from 1995 to 2011. SED was defined as the quartile with the highest Carstairs scores, and was analysed in relation to mortality after stroke in a multivariate-adjusted Cox regression model.

Results: In a follow-up of 17 years, 498 patients died. Compared with the 1st quartile of Carstairs score (the least deprived), the multivariate-adjusted hazard ratios (HRs) for 17-year mortality in patients in the 2nd, 3rd and 4th quartiles were 0.94 (95%CI 0.72-1.23), 1.17 (0.90-1.52) and 1.36 (1.04-1.78), overall p=0.04. The SED gradient association remained in patients with intracerebral haemorrhagic stroke, while in patients with subarachnoid haemorrhagic stroke the corresponding HRs were 2.62 (1.22-5.64), 3.03 (1.49-6.18) and 1.83 (0.87-3.83) respectively. Results of 10-year mortality showed similar patterns, although the association of deprivation with 1-year mortality was not significant.

Conclusions: There is a significant impact of SED on long-term mortality after haemorrhagic stroke. The reasons for this survival inequality must be explored to reduce mortality in patients with haemorrhagic stroke.

INTRODUCTION

People with socioeconomic deprivation (SED) suffer from an increased risk of stroke and functional impairment after stroke,[1, 2] and there is a correlation between stroke incidence and mortality with SED that cannot be completely explained by differences in risk factors.[1] There is growing evidence of a correlation between SED and mortality after ischaemic stroke,[1, 3, 4] however it is less clear whether there is an association of SED with mortality after haemorrhagic stroke, which has different aetiology and treatment strategies than ischaemic stroke. Recent studies have shown conflicting findings regarding this association.[5-7] Most studies have only focused on the short-term impact of SED on survival after haemorrhagic stroke,[5-8] and few studies have compared the impact of SED on survival after intracerebral haemorrhagic stroke (ICH) with subarachnoid haemorrhage (SAH).[5, 6, 9] In this paper we analysed data from a long-term population-based cohort of people with haemorrhagic stroke in the UK to examine the association of SED with mortality after ICH and SAH stroke

METHODS

The data was derived from the South London Stroke Register (SLSR), and the methods have been fully described previously.[2, 10] In brief, the SLSR is an on-going prospective population-based stroke register beginning in 1995, which records all first ever strokes of all residents living in 22 electoral wards in Lambeth and Southwark councils in inner-city South London (total population at the 2001 census was 271,817), using a combination of hospital and community records to include all

cases of incident stroke.[STEWART] Data collected between 1995 and 2011 were used in this analysis.

Sociodemographic Characteristics

Ethnic origin (self-defined, census question) was stratified into White, Black Caribbean, Black African, South Asian (Indian, Pakistani, Bangladeshi), Chinese, other, and unknown. For the purposes of analysis this was then grouped into White, Black, Asian/other and unknown. We calculated the Carstairs deprivation index score[11] based on the patients' postcode of residence at the time of stroke to measure baseline SED for each patient, as has been described previously.[12] The Carstairs index is an area-based measure of socio-economic deprivation derived from decennial census data, using levels of male unemployment, overcrowding, car ownership and proportion in social classes IV and V (partly skilled and unskilled) in a small area.[11, 13] The index was derived using 2001 census data for each lower layer super output area covered by the register. A higher score indicates higher levels of deprivation.[11] The Carstairs deprivation index has been validated and widely used in health-related studies in the UK.[13]

Risk Factors Before Stroke

Risk factors such as hypertension (general practice or hospital records of high blood pressure >140 mm Hg systolic or >90 mm Hg diastolic), myocardial infarction, atrial fibrillation, peripheral vascular disease, previous transient ischemic attack, diabetes mellitus, and current smoking status were recorded by the interview team. Accommodation type was recorded to measure social networks and contact.

Case Mix

The diagnosis of stroke (using the World Health Organization clinical definition) was verified by a study clinician, and patients were examined within 48 hours of being notified to the SLSR where possible.[not delete this sentence]Clinical details were obtained at the time of maximal impairment. Case severity variables included urinary incontinence; swallow impairment; speech deficit; motor deficit; Glasgow Coma Scale, dichotomized to <13 (severe/moderate) and ≥ 13 (mild); and Barthel index at 7 days after stroke, grouped into the following categories based on hospital records or the interview team administering a standard questionnaire: <15 (severe/ moderate disability), 15-19 (mild disability) and 20 (independent disability).

Stroke Subtype

Classification of pathological subtype (cerebral infarction, primary intracerebral haemorrhage, and subarachnoid haemorrhage) was based on results from at least one of the following: brain imaging, cerebrospinal fluid analysis, or necropsy examination. Cases without pathological confirmation of stroke subtype were unclassified.

Acute Care After Stroke

Patients were classified based on admission to hospital, admission to stroke unit, $>50\%$ stay on stroke unit, brain imaging, and swallow test.[10]

Follow-up of the cohort

Follow-up data were collected by validated postal or face-to-face instruments with patients and/or their carers.[10, 14] Patients were assessed at three months and annually after stroke. All follow-up assessments included in the present study were

completed by 31 December 2011.. The vital statuses of the cohort members are monitored on an on-going basis via the Office for National Statistics (ONS).

Statistical Analysis

Median score of Carstairs index was calculated for socio-demographics, cardiovascular risk factors, stroke severity and acute stroke care using a non-parametric Kruskal-Wallis test. To assess the association between SED and mortality, patients were divided into four quartiles based on Carstairs deprivation index score, with the 4th quartile comprising the most deprived patients. Cox regression models were used to compute hazard ratios (HR) and 95% confidence intervals for mortality after haemorrhagic stroke in relation to SED, with the least deprived quartile (Q1) serving as a reference for comparison with the more deprived quartiles (Q2, Q3, Q4). HRs were adjusted for socio-demographics (age, sex, ethnicity, year of stroke, admission to hospital, accommodation type prior to stroke), cardiovascular disease risk factors (smoking status, hypertension, myocardial infarction, atrial fibrillation, diabetes, peripheral vascular disease, transient ischaemic attack), Barthel index prior to stroke, and stroke severity (Glasgow coma scale score, speech deficit, motor deficit). To test whether acute stroke care played a mediating effect on the association, we further adjusted for variables of hospital admission, stroke unit admission, >50% of stay on stroke unit, brain imaging and swallow test. We tested these variables in the modelling for little collinearity. We examined mortality at 1 year, 10 years and 17 years follow-up.

Ethics

Patients or their relatives gave written informed consent to participate in this study. Ethical approval was obtained from the ethics committees of Guy's and St. Thomas'

Hospital Trust, King's College Hospital, Queens Square, and Westminster Hospital (London).

RESULTS

There were 4398 patients registered with the SLSR from 1995-2011, 784 of which had a primary haemorrhagic stroke. 782 patients with haemorrhagic stroke had SED data available for analysis. Characteristics of these patients are shown in Table 1 (appendix) with median Carstairs score and interquartile ranges. Carstairs scores were higher in patients who currently smoked, were admitted to St. George's hospital, did not have speech deficits after stroke, were not admitted to a stroke unit, and did not stay in the unit for >50% of their hospitalisation.

In the 17 year follow-up 498 patients died. Hazard ratios (HR) and 95% confidence intervals for mortality of patients by Carstairs quartiles are presented in Table 2, with separate data analysis for mortality after 1, 10 and 17 years follow-up. Compared with the 1st quartile of Carstairs score (the least deprived), the adjusted HR for 17-year mortality in patients in the 4th quartile was 1.30 (95% CIs 1.00-1.68), overall $p=0.07$. After further adjustment for acute stroke care, the association was not substantially changed, however the overall p -value became significant at $p=0.04$ (Table 2). Data of 10-year mortality showed similar patterns of association, but the association of SED with 1-year mortality after stroke was not significant (Table 2).

Over the 17 year follow-up, 384 of 562 patients with ICH died (68.3%) and 114 of 220 patients with SAH died (51.8%). The social gradient association with 17-year mortality seen in all haemorrhagic stroke patients remained in ICH patients. SAH patients had higher HRs across all quartiles than ICH patients and an overall $p=0.01$, however while the increase in mortality in the 2nd and 3rd quartiles was significant, the

association in the 4th quartile was not (Table 3). The different patterns of association of mortality and SED in ICH and SAH patients were also seen in analysis for 1-year and 10-year mortality after stroke (Table 3).

Table 2. Mortality* and Multivariate Adjusted HR[†] of Haemorrhagic Stroke Patients Across 4 Quartiles of Carstairs Scores: SLSR

Carstairs Quartile	Duration of follow-up								
	1 Year			10 Years			17 Years		
	Death (%)	HR [†] (95% CI)	p	Death (%)	HR [†] (95% CI)	p	Death (%)	HR [†] (95% CI)	p
Adjusted Model I [†]									
Q1 (least deprived)	87 (43.9)	1.00	0.55	112 (56.6)	1.00	0.06	120 (60.6)	1.00	0.07
Q2	87 (44.6)	0.93 (0.68-1.28)		119 (61.0)	0.94 (0.72-1.23)		125 (64.1)	0.92 (0.71-1.20)	
Q3	97 (49.2)	1.07 (0.79-1.44)		124 (62.9)	1.13 (0.87-1.47)		128 (65.0)	1.12 (0.87-1.45)	
Q4 (most deprived)	87 (45.3)	1.16 (0.86-1.58)		122 (63.5)	1.33 (1.02-1.73)		125 (65.1)	1.30 (1.00-1.68)	
Adjusted Model II €									
Q1 (least deprived)	87 (43.9)	1.00	0.30	112 (56.6)	1.00	0.03	120 (60.6)	1.00	0.04
Q2	87 (44.6)	0.96 (0.70-1.32)		119 (61.0)	0.96 (0.73-1.27)		125 (64.1)	0.94 (0.72-1.23)	

Q3	97 (49.2)	1.17	(0.86-1.59)	124 (62.9)	1.19	(0.91-1.56)	128 (65.0)	1.17	(0.90-1.52)
Q4 (most deprived)	87 (45.3)	1.26	(0.91-1.73)	122 (63.5)	1.40	(1.07-1.85)	125 (65.1)	1.36	(1.04-1.78)

* the number of patients at the specified follow-up time were only those who were actually followed up for that amount of time that time, including deaths (ie. Cases occurring less than ten years prior to the end of the data collection period would only be included in the one-year follow up calculation).

† adjusted for age, sex, ethnicity, year of stroke, accommodation type prior to stroke, admitted to hospital, smoking status, hypertension, myocardial infarction, atrial fibrillation, diabetes, peripheral vascular disease, transient ischaemic attack, stroke subtype (for all haemorrhagic stroke only), Glasgow coma score, speech deficit and motor deficit.

€ adjusted for all variables above and plus hospital admission, stroke unit admission, >50% of stay on stroke unit, brain imaging and swallow test

‡ Overall *p* value for the variable

Table 3. Mortality* and Further Multivariate Adjusted HR[†] of Patients with ICH and SAH Across 4 Quartiles of Carstairs Scores: SLSR

Duration of follow-up										
Carstairs Quartile	1 Year			10 Years			17 Years			
	Death	HR [†] (95%CI)	p	Death (%)	HR [†] (95%CI)	p	Death (%)	HR [†] (95%CI)	p	
	(%)									
ICH patients										
Q1 (least deprived)	65 (45.1)	1.00	0.27	89 (61.8)	1.00	0.03	95 (66.0)	1.00	0.03	
Q2	61 (42.6)	0.87 (0.60-1.27)		90 (62.9)	0.88 (0.64-1.20)		94 (65.7)	0.85 (0.63-1.16)		
Q3	69 (50.7)	1.09 (0.75-1.58)		90 (66.2)	1.04 (0.76-1.42)		92 (67.7)	1.02 (0.75-1.38)		
Q4 (most deprived)	70 (50.4)	1.26 (0.87-1.81)		101 (72.7)	1.39 (1.02-1.88) ¹		103 (74.1)	1.34 (1.00-1.81)		
SAH patients										

Q1 (least deprived)	22 (40.7)	1.00		0.10	23 (42.6)	1.00		0.01	25 (46.3)	1.00		0.01
Q2	26 (50.0)	2.30	(1.05-5.03)		29 (55.8)	2.62	(1.22-5.64)		31 (59.6)	2.50	(1.19-5.28)	
Q3	28 (45.9)	2.28	(1.10-4.70)		34 (55.7)	3.03	(1.49-6.18)		36 (59.0)	2.96	(1.50-5.87)	
Q4 (most deprived)	17 (32.1)	1.54	(0.71-3.37)		21 (39.6)	1.83	(0.87-3.83)		22 (41.5)	1.74	(0.85-3.56)	

* the number of patients at the specified follow-up time were only those who were actually followed up for that amount of time that time, including deaths (ie. Cases occurring less than ten years prior to the end of the data collection period would only be included in the one-year follow up calculation).

† adjusted for age, sex, ethnicity, year of stroke, accommodation type prior to stroke, admitted to hospital, smoking status, hypertension, myocardial infarction, atrial fibrillation, diabetes, peripheral vascular disease, transient ischaemic attack, stroke subtype (for all haemorrhagic stroke only), Glasgow coma score, speech deficit, motor deficit, hospital admission, stroke unit admission, >50% of stay on stroke unit, brain imaging and swallow test.

‡ Overall *p* value for the variable

DISCUSSION

We observed an SED gradient with mortality in a multi-ethnic population stroke register in the UK, with the highest long-term mortality after haemorrhagic stroke in the most deprived quartile of the population. The significant association of SED with mortality remained even after adjustment for acute stroke care variables. By performing separate analyses by subtype of haemorrhagic stroke, we found that long-term mortality was associated with both ICH and SAH stroke, however a gradient was only observed for ICH.

Previous studies have suggested that SED is significantly associated with increased mortality after ischemic stroke,[1, 3] however research to date regarding haemorrhagic stroke has shown inconsistent findings. The voluntary MRFIT cohort in the USA reported 139 SAH fatalities after a follow-up period of 11 years, and observed an association between higher mortality in higher income quintiles after adjustment for demographics and cardiovascular risk factors, however this was not statistically significant, and the reverse trend was found in patients with ICH.[9] Cesaroni et. al looked at a cohort with 920 fatalities due to haemorrhagic stroke in Italy and found a non-significant positive association between SED and mortality 1 year after stroke in the middle three SED quintiles in men (but not the most deprived quintile), and in the second, third and bottom (most deprived) quintile in women.[8] Fukada et. al looked at death registration records in Japan and found 272,590 fatalities due to haemorrhagic stroke over two 5-year periods. There was a strong, significant trend of increasing mortality in those in the lower socioeconomic positions, measured by income and

education.[15] More recently, a cohort of the working population in Sweden with 2619 fatalities due to ICH over a 12 year period displayed a strong significant association between lower income and higher mortality, after adjustment for demographics, education, and occupation.[16]

These inconsistencies may be due to the variation in populations studied, methodology in measuring socioeconomic status (SES), subtype of haemorrhagic stroke assessed, and the length of follow-up. Our study used a composite SES indicator, assessed both ICH and SAH separately, and looked at short- and long-term follow-up. It has shown that the association between SED and reduced survival in long term follow-up after haemorrhagic stroke is significant.

Clear, significant gradients have been reported in previous studies that have examined mortality after SAH.[7, 17, 18] We did not find a social gradient association in patients with SAH, despite higher mortality in the middle two quartiles; this may be due to small sample size, as there were only 22 fatalities occurring after a 17-year follow-up in the 4th quartile of SAH patients. Given the higher HRs and levels of significance in the 2nd and 3rd quartiles of SAH patients, studies with larger sample sizes may find that the 4th quartile will have significantly increased mortality, which would contribute to a larger overall association between SED and mortality in all haemorrhagic stroke patients. Larger studies are needed to examine this trend in SAH patients.

Our data of 1-year mortality did not show a significant association. This may be due to the relatively lower number of deaths that had occurred after only one year, however some previous studies have seen an association earlier than 1 year in some populations

and SED groups. In the FINMONICA Stroke Register cohort with 909 ICH patients and 503 fatalities, Jakovljevic et. al found that compared with the highest income group, the odds ratio (adjusted for age, study area and urban/rural residence) in older male patients (aged 60-74) with the middle and the lowest income were 1.81 (0.74-4.40) and 2.40 (1.04-5.55), respectively.[5] The increased trend was also observed in younger men where both lower income tertiles were significant, and in women aged 25-59 (not significant), but not in women 60-74, where the middle tertile had lower mortality than both the highest and lowest income groups. Only some of these populations tested had statistically significant trends, and it is possible the sample size of the populations examined were too small. Conversely, Cesaroni et. al did not show a significant association between SED and mortality after 30 days or one year after haemorrhagic stroke, despite a larger sample size.[8] The impact of SED on short-term mortality needs to be further investigated.

A major strength of this study is the length of the cohort follow-up, which is unprecedented in representative population-based cohorts in this field. To our knowledge, this cohort had the longest follow-up period of any cohort examining the association of SES and mortality after haemorrhagic stroke; the study with the longest length of follow-up prior to this being the 16-year follow-up of the voluntary MRFIT cohort examining 35-57 year old men in the USA beginning in the early 1970's, which only measured a total of 320 fatalities.[19, 20] We have also examined ICH and SAH separately, and identified the association that is seen between SED and mortality in all haemorrhagic stroke as coming mainly from ICH patients.

Our study has several limitations. Firstly, despite a large cohort, our sample was not large, due to the low relatively incidence of haemorrhagic stroke. Secondly, we did not adjust for processes of care, recurrent stroke, and incident co-morbidities which occurred during the follow-up period, as they could be related to baseline acute stroke care and adjustment may cause collinearity problems. Stroke severity and acute stroke care were included in our adjustments, therefore any confounding by the aforementioned variables would be lessened, however as we found significant differences in SED and markers of acute care in our cohort, it is likely there is still residual confounding due to unequal acute- and long-term care across socioeconomic groups. Thirdly, [see and use these from the revised response letter] data was missing for a number of risk factors for some cases. This affected the ability of our model to fully adjust for these risk factors (eg. Speech deficit, where 30% are unknown). Not fully adjusting for risk factors may affect the estimation of the association between SED and mortality, however only four of 23 variables have more than 10% of cases with missing data, suggesting any over or underestimation of association is limited. Lastly, caution should be used when generalising the study findings to other populations. The SLSR cohort data was collected in inner-city South London only, which has differing population demographics and health compared to other populations in the UK and internationally, thus our results may not be applicable to other populations. In addition, Carstairs deprivation index was used as a measure of SES, but we were not able to include other common socioeconomic measures such as income or education. Studies in this field use a mix of either income, education, or composite indices, and including education and income data would allow our study to

Comment [A1]: Can we do sensitivity analysis? Is it possible to see if the data is missing equally by SED groups?

be more generalisable, as well as help to examine the effect of different aspects of SES on mortality after haemorrhagic stroke.

In conclusion, our study reported the impact of SED on mortality after haemorrhagic stroke in a population-based stroke register in the UK. Compared to the least deprived group, the most deprived had an increased risk of long-term mortality after haemorrhagic stroke. This increase in mortality appears to be independent of socio-demographics, cardiovascular risk factors, stroke severity, and acute stroke care. Our findings contribute to the evidence that there are inequalities in survival after haemorrhagic stroke. Further research is required to investigate the cause for these inequalities, and to determine action to reduce associated mortality.

Comment [A2]: Soften as missing variables

MAIN MESSAGES

- Socioeconomic deprivation is associated with increased mortality after haemorrhagic stroke, with a clear deprivation gradient 17 years after stroke, and appears to be independent of socio-demographics, cardiovascular risk factors, stroke severity, and acute stroke care.
- There has previously been conflicting evidence regarding the effect of socioeconomic status on mortality after haemorrhagic stroke, with a number of studies examining differing populations with varying results.
- The effect of socioeconomic status on mortality differs between intracerebral haemorrhage and subarachnoid haemorrhage; further research is required to determine the mechanisms behind this.

REMAINING RESEARCH QUESTIONS:

- How does the difference in aetiology between stroke subtypes affect the difference in the effect of socioeconomic status on mortality after stroke?
- Why is there a difference between the association of socioeconomic status and mortality in the short term and the long term?
- By what mechanism does socioeconomic status affect mortality after haemorrhagic stroke?

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COMPETING INTERESTS

None.

CONTRIBUTORSHIP STATEMENT

JM analysed and interpreted the data, and wrote the manuscript as a part of a Master's of Public Health dissertation. RC provided the secondary data from the South London Stroke Register according to an agreement with the Division of Health and Social Care, KCL on the MPH study programme, advised on the study design and analysis, and contributed to the writing of the manuscript.

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